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B164 - EBV REACTIVATION ASSOCIATED POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE, CLONAL GAMMOPATHY AND OUTCOMES IN ALLOGENEIC T-CELL DEPLETED STEM CELL TRANSPLANTS FOR MYELOID MALIGNANCIES

Varun Mehra¹, Eleanor Barnwell¹, Ute Boczek¹, Stefani Widya², Adrian Choy², Alessandra Bisquera³, Kavita Raj^{1,4}, Donal McLornan^{1,4}, Shreyans Gandhi¹, Austin Kulasekararaj¹, Hugues de Lavallade¹, Victoria Potter¹, Ghulam Mufti^{1,2}, Antonio Pagliuca¹
¹Kings College Hospital, Haematology, London, United Kingdom, ²GKT School of Medicine, London, Haematology, London, United Kingdom, ³King's College London, Division of Health and Social Care Research, London, United Kingdom, ⁴Guy's and St Thomas' Hospital, Haematology, London, United Kingdom

Background: Epstein Barr Virus is frequently reactivated (EBV-R) in immunocompromised allogeneic haematopoietic stem cell transplant (HSCT) patients following T cell depletion (TCD). Incidental observations of monoclonal gammopathy (MG or M-protein) post-HSCT have also been reported. We report on incidence & outcomes of EBV-R, PTLD and association with M-protein in a large cohort of in-vivo TCD allogeneic HSCTs and provide quantitative underpinning to decisions about pre-emptive treatment for post-transplant lymphoproliferative disease (PTLD).

Methods: This is a single-centre retrospective analysis of 293 consecutive patients who underwent TCD allo-HSCTs for myeloid malignancies between January 2012-June 2016. EBV-DNA was monitored frequently on whole blood samples with standardised quantitative real-time PCR. Serum protein electrophoresis was routinely tested with immunoglobulin subclasses identified by immunofixation electrophoresis. Histological confirmation of PTLD was based on standard WHO diagnostic criteria ('proven'), while those without biopsy were classed as 'probable' based on clinical & radiological criteria as defined by ECIL-6 guidelines.

Results: Majority of patients had AML (n=152/293) and MDS (n=107/293) with a median age of 58 years (range 22-76). Median follow up of survivors was 32 months (range 4-65). Majority of patients (n=220/293; 75%) developed EBV-R with a median time of 79 days [Inter quartile range (IQR) 27-160 days] & higher cumulative incidence with ATG (n=132) versus Alemtuzumab (n=161) ($p < 0.001$). **Figure-1a** shows schematic representation of EBV and PTLD events (cumulative incidence of 6.8% (95%CI-4.0%-10.6%) at 12 months). Significantly higher peak EBV DNA viral load (EVL) were noted in patients with PTLD ($p < 0.001$). Development of post-HSCT MG was observed in 29% (n=85/292). ROC curve identified peak blood EVL > 150,000 copies/ml significantly correlated with risk of developing PTLD (sensitivity-70.6%, specificity-79.4%; AUC-0.82, $p < 0.001$). Based on these estimates, subgroup of patients with no EBV-R (n=72/292), peak EVL < 150,000 (< 150k) copies/ml (n=165/292) & > 150,000 (> 150k) copies/ml (n=55/292) were categorised in 6 groups along patients with/without MG accordingly (**Groups 1-6; Figure-1b**). Patients with EBV-R had significantly better OS [5-year OS of 52% vs 35% (no EBV-R); Log-rank $p < 0.001$], with

this survival benefit mainly driven by subgroup of patients with lower EVL(< 150k)($p < 0.001$). PTLT patients had trend towards inferior 3-year OS(15% vs 54%; $p = 0.051$). Patients with MG had a significantly better OS irrespective of degree of EVL(Group 1-3, $p < 0.001$). We report a 'sweet spot' of low EVL & presence of MG in these patients, with a clear survival advantage compared to those with no EBV-R and/or no M-protein (Group-2 5-year OS 62% vs 27% in Group-6; HR-0.15;95%CI:0.06-0.34; $p < 0.001$; **Figure1b**). Overall cumulative incidence of relapse (CIR) was 28%(95%CI:23-37) and non-relapse-mortality(NRM) of 24%(95%CI:18.6-30) at 5 years. Multivariate analysis(MVA) revealed absence of M-protein, high EVL (>150k copies/ml) or no EBV-R and absence of any GVHD as significant factors for high CIR. Similarly, high EVL or no EBV-R, absence of M-protein and ITU admission were significant predictors of high NRM.

Conclusions: This study adds to our understanding of role of EBV viraemia & associated MG in TCD-HSCTs while highlighting its significant impact on risk of PTLT, OS, NRM & CIR. Low EBV burden and development of MG is protective with significantly better survival outcomes and we recommend pre-emptive approach of using Rituximab for EBV-R /PTLT is best employed at higher EBV burden (e.g. >150k copies/ml DNA) in high risk patients and be prospectively evaluated in future studies.

Figure 1a: Schematic representation of EBV reactivation and PTLD events.

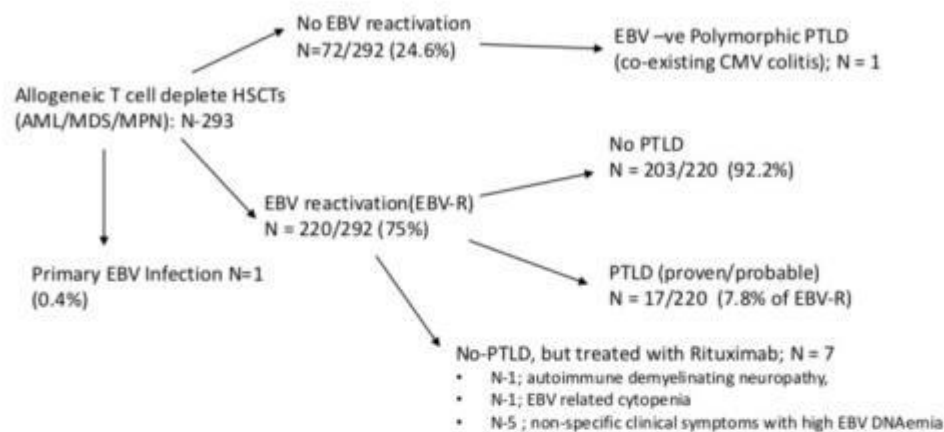
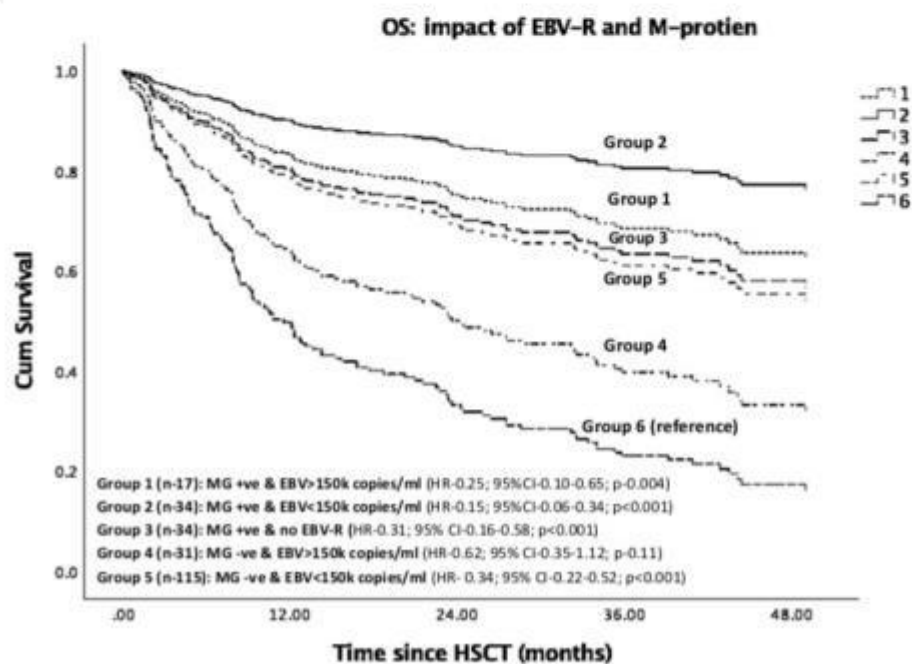


Figure 1b: Overall Survival with Monoclonal Gammopathy and peak EBV viraemia burden (Group 1-6)



[[P393 Image] 1. Figure 1a-1b]

Clinical Trial Registry: n/a

Disclosure: Nothing to declare

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